UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte DEBORAH CHARYCH, ERIC BEAUSOLEIL, and RONALD N. ZUCKERMANN

Appeal 2007-2723
Application 09/874,091
Technology Center 1600

Decided: November 8, 2007

Before ERIC B. GRIMES, RICHARD M. LEBOVITZ, and FRANCISCO C. PRATS, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to an array of protein binding agents attached to a solid support. The Examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

BACKGROUND

"In recent years, microarray technology has developed from a specialized sub-field into an important tool for basic and applied studies in molecular biology, microbiology, pharmaceutics, agriculture, and many

other biotechnologies. DNA microarray technology attempts to link the genome of an organism or cell to an expressed phenotype or protein function" (Specification 1).

However, using DNA microarrays to evaluate a cell can be problematic because, "[i]n many cases, functional pathways cannot be directly linked to a particular gene. Proteins often undergo a variety of post-translational modifications, interactions, or degradations that ultimately determine function" (*id.* at 2). Thus, "[e]ven the seemingly simple evaluation of a protein's abundance cannot be directly correlated with the level of corresponding mRNA. The only solution is to evaluate the state of the cell, tissue or organism at the protein level" (*id.*).

DISCUSSION

1. CLAIMS

Claims 1, 60-73, 79-91, and 97-101 are pending and on appeal (Appeal Br. 1). Claims 1 and 73, the two appealed independent claims, are representative and read as follows:

> 1. An array of protein-binding agents stably attached to the surface of a solid support, said array comprising:
>
> a solid substrate having a substantially planar surface comprising a layer of aluminum formed on a glass base material, the aluminum coated with a silicon dioxide coating having a thickness of between about 200 and 900Å;
>
> a plurality of different protein-binding agents bound to said substrate, each of said protein-binding agents comprising,
>
> an anchoring segment stably bound to the substrate surface,
>
> a peptidomimetic protein-binding segment, and
>
> a linker segment connecting and separating the anchoring and peptidomimetic segments.

73. A kit for use in performing a differential binding assay, said kit comprising:

an array comprising

a solid substrate having a substantially planar surface comprising a layer of aluminum formed on a glass base material, the aluminum coated with a silicon dioxide coating having a thickness of between about 200 and 900 Å;

a plurality of different protein-binding agents bound to said substrate, each of said protein-binding agents comprising,

an anchoring segment stably bound to the substrate surface,

a peptidomimetic protein-binding segment, and

a linker segment connecting and separating the anchoring and peptidomimetic segments;

one or more reagents for conducting a differential binding assay comprising a plurality of fluorescent labels for proteins.

2. PRIOR ART

The Examiner relies on the following references:

Gustafson	US 5,478,527	Dec. 26, 1995
Barrett	US 5,482,867	Jan. 9, 1996
Chenchik	US 6,087,102	Jul. 11, 2000
Wagner	US 6,329,209 B1	Dec. 11, 2001

3. OBVIOUSNESS -- GUSTAFSON AND CHENCHIK

Claims 1, 60, 61, 63-66, 73, 79, 80, 82-85, and 97-101 stand rejected under 35 U.S.C. § 103 as obvious in view of Gustafson and Chenchik (Answer 3-6, 13-16).

The Examiner cites Gustafson as teaching a "biograting" that comprises protein binding agents attached in a patterned arrangement to a wafer composed of glass, aluminum, and silicon dioxide layers that meet the limitations recited in claim 1 (*id.* at 3-4). With respect to claim 1 and its dependents, the Examiner states that "[t]he array of Gustafson et al. differs from the presently claimed invention by failing to include a plurality of fluorescent labeled proteins" (*id.* at 4). With respect to claim 73 and its dependents, the Examiner states that Gustafson "differs from the presently claimed invention by failing to include packaging the array into a kit format that includes a label[ed] reagent" (*id.* at 14).

The Examiner cites Chenchik to meet those limitations (*id.* at 4-5, 14-15). The Examiner finds that persons of ordinary skill in the art would have been motivated to incorporate Chenchik's plurality of fluorescently labeled proteins into Gustafson's array "for the advantage of providing a high throughput format that provides two types of informations, which are the types of genes expressed and the size of the expressed products[,] since both Gustafson et al. and Chenchik et al. disclose an array of polymeric compounds such as proteins" (*id.* at 5, citations omitted). The Examiner finds that the same rationale would have encouraged one of ordinary skill to package Gustafson's assay product in a kit having a plurality of fluorescently labeled proteins (*id.* at 15).

Appellants argue that the combination of references advanced by the Examiner would not have rendered the claims obvious because "Gustafson relates to such fundamentally different arrays and assay techniques than both Chenchik and the claimed invention that one of skill would not arrive at the

claimed invention from the combination of Gustafson and Chenchik" (Br. 7-8).

> In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. "[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references."

In re Fritch, 972 F.2d 1260, 1265 (Fed. Cir. 1992) (citations omitted, bracketed material in original). Thus, as recently pointed out by the Supreme Court, "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007). Rather, "[t]he test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art." *In re Young*, 927 F.2d 588, 591 (Fed. Cir. 1991).

We agree with Appellants that the Examiner has not established that the teachings of Gustafson and Chenchik would have led one of ordinary skill to practice the subject matter recited in the rejected claims.

Specifically, the only difference between Gustafson and claim 1 acknowledged by the Examiner is Gustafson's "fail[ure] to include a plurality of fluorescent labeled proteins" (Answer 4). With respect to claim 73, the only difference acknowledged by the Examiner is that Gustafson "fail[s] to include packaging the array into a kit format that includes a label[ed] reagent" (*id.* at 14). However, claims 1 and 73 both require "a

plurality of *different* protein-binding agents" (emphasis added) to be bound to the claimed array's substrate.

We do not see, and the Examiner does not explain, where Gustafson discloses or suggests a substrate having a plurality of different protein-binding agents. Specifically, Gustafson discloses a "biograting," which is a flat surface coated with "a diffraction grating pattern of alternating and preferably parallel linear zones of an active and deactivated binding reagent. The zones form a diffraction grating when the active binding reagent binds with its opposite member of the binding pair" (Gustafson, col. 3, ll. 60-64; *see also* Figure 1). Thus, when a target analyte present in a sample binds to the substrate-bound protein binding agent "the accumulation of bound material in the patterns of a diffraction grating creates a light disturbing grating, and light detected at the light diffraction angles increases to a large value which correlates to the presence and quantity of the binding partner (analyte) in the sample" (*id.* at col. 3, l. 67, through col. 4, l. 5). In contrast, because a sample lacking the target analyte will contain nothing that can bind to the substrate-bound active binding reagent, "no significant light diffraction occurs, that is, light energy detected at the diffraction angles is at a minimum value, approaching zero" (*id.* at col. 3, ll. 64-67).

Thus, Gustafson's substrate contains only a single type of protein binding agent attached to it in a pattern that, when bound with a protein binding partner, diffracts light in a manner that allows for detection and quantification of a target analyte (*id.* at col. 3, l. 56 through col. 4, l. 5). We therefore agree with Appellants that Gustafson does not describe how to use

its grating with different protein binding partners (Appeal Br. 10). To the contrary, "the entire context of Gustafson is premised on a single target bound on a substrate densely enough to form parallel lines that will diffract incident light when bound to its analyte partner" (*id.*).

To reflect sufficient light to evaluate the light diffraction, Gustafson discloses that the underlying substrate should have a "reflective [] layer . . . supported on an optically flat surface of a wafer, and the reflective metal can be aluminum" (*id.* at col. 2, ll. 44-46). A layer of silicon dioxide, to which the protein binding agent will be attached, is "[p]referably . . . formed by sputtering a thin layer of silicon dioxide or by coating an alkali metal silicate solution on the surface of the reflective metal" (*id.* at col. 2, ll. 48-50). Therefore, to the extent that Gustafson discloses or suggests a substrate meeting the structural limitations in claims 1 and 73, Gustafson also discloses that that substrate is designed to reflect light in a manner such that a single analyte bound to the substrate in a patterned arrangement will diffract light in a detectable and quantifiable manner.

Unlike Gustafson, Chenchik is not directed to detecting a single analyte based on the light diffraction that results when the analyte binds to a patterned substrate-bound binding partner. Instead, Chenchik uses fluorescently labeled proteins to determine when binding has occurred between one of the arrays' different substrate-bound protein-binding agents and its partner (*see* Chenchik, col. 8, l. 55, through col. 11, l. 24).

Because Chenchik's fluorescence-based detection techniques do not rely on light diffraction to detect the presence of a target analyte, we agree with Appellants that one of ordinary skill would not have looked to

Gustafson's diffraction-generating biograting substrate as a support for Chenchik's protein-binding arrays. We also agree with Appellants that, because Gustafson discloses that the detectable light diffraction requires a single analyte to be bound to the substrate in a specific pattern, one of ordinary skill would not have considered it obvious to attach a plurality of different protein-binding agents to Gustafson's substrate.

Therefore, because the Examiner has not shown that persons of ordinary skill in the art would have been prompted to attach a plurality of different protein-binding agents to a substrate having the claimed glass/aluminum/silicon dioxide configuration, we reverse the Examiner's obviousness rejections of claims 1 and 73, and their dependent claims.

4. OBVIOUSNESS -- GUSTAFSON, CHENCHIK, AND WAGNER

Claims 62 and 81 stand rejected under 35 U.S.C. § 103 as obvious over Gustafson, Chenchik, and Wagner (Answer 6-10, 16-20).

Claim 62, ultimately depending from claim 1, limits the array of claim 1 to one having a maleimide-functionalized aminosilane between the silicon oxide layer and the protein binding agents. Claim 81, ultimately depending from claim 73, limits the array in the kit of claim 73 to one having the same maleimide-functionalized aminosilane linkage between the silicon oxide layer and the protein binding agents.

The Examiner concedes that Gustafson and Chenchik do not disclose an array having the feature recited in claims 62 and 81, and cites Wagner to meet that limitation (Answer, 8-9, 18-19). We reverse this rejection as well. As discussed above, we do not agree with the Examiner that one of ordinary skill would have considered the arrays recited in claims 1 and 73 obvious in

view of Gustafson and Chenchik. We do not see, and the Examiner does not point to, any disclosures in Wagner that remedy the shortcomings of the other references.

We therefore reverse the Examiner's rejections of claims 62 and 81.

5. OBVIOUSNESS -- GUSTAFSON, CHENCHIK, AND BARRETT

Claims 67-72 and 86-91 stand rejected under 35 U.S.C. § 103 as obvious over Gustafson, Chenchik, and Barrett (Answer 10-13, 20-23).

Claim 67, ultimately depending from claim 1, limits the array of claim 1 to one having an avidin-functionalized aminosilane between the silicon oxide layer and the protein binding agents. Claim 68 depends from claim 67, and limits the array's anchoring segment to biotin. Claims 71, 72, 86, 87, 90, and 91 contain similar limitations. The Examiner concedes that Gustafson and Chenchik do not disclose an array having the features recited in the rejected claims, and cites Barrett to meet those limitations (Answer, 12-13, 22-23). We reverse this rejection as well.

We first note that claims 69, 70, 88, and 89 do not recite the avidin-biotin linkage which the Examiner cites as being disclosed by Barrett. Rather, those claims appear to recite the maleimide-derivatized aminosilane for which the Examiner cited the Wagner reference. Thus, the references cited by the Examiner do not appear to disclose all of the limitations of the claims included in this ground of rejection.

Moreover, as discussed above, we do not agree with the Examiner that one of ordinary skill would have considered the arrays recited in claims 1 and 73 obvious in view of Gustafson and Chenchik. Because we do not see, and the Examiner does not point to, any disclosures in Barrett that remedy

the shortcomings of the other references, we reverse the Examiner's obviousness rejections of claims 67-72 and 86-91.

SUMMARY

We reverse the Examiner's obviousness rejections of claims 1, 60-73, 79-91, and 97-101.

REVERSED

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